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*Admitted only in Maryland
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April 26, 2002

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Commissioner for Patents
Washington, D.C. 20231

Art Unit: 1652

Re: U.S. Utility Patent Application
Appl. No. 10/045,072; Filed: January 15, 2002
For: **Pyruvate Carboxylase from *Corynebacterium Glutamicum***
Inventors: SINSKEY *et al.*
Our Ref: 1533.0790002/MAC/AGU

Sir:

Transmitted herewith for appropriate action are the following documents:

1. Information Disclosure Statement;
2. Form PTO-1449, 15 pages, listing 47 documents;
3. One copy of each of the 47 cited documents on Form PTO-1449; and
4. Return postcard.

It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier. In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

Commissioner for Patents
April 26, 2002
Page 2

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Michele A. Cimbala
Attorney for Applicants
Registration No. 33,851

MAC/AGU/jk
Enclosures

SKGF_DC1:6807.1



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Sinskey *et al.*

Appl. No. 10/045,072

Filed: January 15, 2002

For: **Pyruvate Carboxylase from
Corynebacterium Glutamicum**

Confirmation No. 3733

Art Unit: 1652

Examiner: *To Be Assigned*

Atty. Docket: 1533.0790002/MAC/AGU

#4
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4/30/02

Information Disclosure Statement

Commissioner for Patents
Washington, D.C. 20231

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Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98. A copy of each of these documents is provided.

In accordance with 37 C.F.R. § 1.98(a)(3), Applicants' undersigned representative submits the following, in regards to non-English language document AM1 cited on Form PTO 1449:

Document **AM1**, WO 99/18228, is in a foreign language. An English language abstract of document **AM1** is attached as document **AR15**. Document **AM1** appears to disclose microbial production of amino acids of the asparate and/or glutamate families comprising increasing pyruvate carboxylase activity by genetic alteration of the enzyme and/or increasing expression of the pyruvate carboxylase gene in appropriate microorganisms.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed publication dates on the attached PTO-1449 based on information presently available to the undersigned. However, the listed publication dates

should not be construed as an admission that the information was actually published on the date indicated.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent application does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith. It is further understood that the Examiner will consider information that had been cited or submitted to the U.S. Patent and Trademark Office in a prior application relied on under 35 U.S.C. § 120. 1138 OG 37, 38 (May 19, 1992).


It is respectfully requested that the Examiner initial and return a copy of the enclosed PTO-1449, and to indicate in the official file wrapper of this patent application that the documents have been considered.

This Information Disclosure Statement is being filed before the mailing date of a first Office Action on the merits. No statement or fee is required.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.


Michele A. Cimbala
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Date: Apr. 26, 2002

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U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB- CLASS	FILING DATE
	AA1	4,275,157	06/23/1981	Tosaka et al.	435	115	07/10/1979
	AB1	6,171,833	01/09/2001	Sinskey et al.	435	183	12/23/1998
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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB- CLASS	TRANSLATION
	AL1	EP 0 723 011	07/24/1996	Europe			Yes No
	AM1	WO 99/18228	04/15/1999	WIPO			Yes X No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	<u>1</u>	Altschul, S.F. et al., "Basic Local Alignment Search Tool," J. Mol. Biol. 215:403-410, Academic Press, Inc., New York, NY (1990).
AS	<u>1</u>	Attwood, P.V., "The Structure and the Mechanism of Action of Pyruvate Carboxylase," Int. J. Biochem. Cell Biol. 27:231-249, Pergamon Press, Exeter, England (1995).
AT	<u>1</u>	Brewster, N.K. et al., "Regulation of Pyruvate Carboxylase Isozyme (PYC1, PYC2) Gene Expression in <i>Saccharomyces cerevisiae</i> during Fermentative and Nonfermentative Growth," Arch. Biochem. Biophys. 311:62-71, Academic Press, New York, NY (1994).

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	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	2	Charles, A.M. and Willer, D.W. "Pyruvate carboxylase from <i>Thiobacillus novellus</i> : properties and possible function," <i>Can. J. Microbiol.</i> 30:532-539, National Research Council Of Canada, Ottawa, Canada (1984).
	AS	2	Dunn, M.F. et al., "Pyruvate Carboxylase from <i>Rhizobium etli</i> : Mutant Characterization, Nucleotide Sequence, and Physiological Role," <i>J. Bacteriol.</i> 178:5960-5970, American Society for Microbiology, Baltimore, MD (1996).
	AT	2	Fry, D.C. et al., "ATP-binding site of adenylate kinase: Mechanistic implications of its homology with ras-encoded p21, F ₁ -ATPase, and other nucleotide-binding proteins," <i>Proc. Natl. Acad. Sci. USA</i> 83:907-911, National Academy of Sciences of the USA, Washington, D.C. (1986).

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>3</u>	Gubler, M. et al., "Effects of phosphoenol pyruvate carboxylase deficiency on metabolism and lysine production in <i>Corynebacterium glutamicum</i> ," Appl. Microbiol. Biotechnol. 40:857-863, Springer-Verlag, Berlin, Germany (1994).
	AS	<u>3</u>	Hanahan, D., "Studies on Transformation of <i>Escherichia coli</i> with Plasmids," J. Mol. Biol. 166:557-580, Academic Press, Inc., New York, NY (1983).
	AT	<u>3</u>	Jäger, W. et al., "A <i>Corynebacterium glutamicum</i> gene encoding a two-domain protein similar to biotin carboxylases and biotin-carboxyl-carrier proteins," Arch. Microbiol. 166:76-82, Springer-Verlag, Berlin, Germany (1996).

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	AL						Yes No
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	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	4	Jetten, M.S.M. and Sinskey, A.J., "Characterization of phosphoenolpyruvate carboxykinase from <i>Corynebacterium glutamicum</i> ," <i>FEMS Microbiol. Lett.</i> 111:183-188, Elsevier/North Holland, Amsterdam (1993).
	AS	4	Keilhauer, C. et al., "Isoleucine Synthesis in <i>Corynebacterium glutamicum</i> : Molecular Analysis of the <i>ilvB-ilvN-ilvC</i> Operon," <i>J. Bacteriol.</i> 175:5595-5603, American Society for Microbiology, Baltimore, MD (1993).
	AT	4	Koffas, M.A.G. et al., "Sequence of the <i>Corynebacterium glutamicum</i> pyruvate carboxylase gene," <i>Appl. Microbiol. Biotechnol.</i> 50:346-352, Springer-Verlag, Berlin, Germany (September 1998).

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	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>5</u>	Koffas, M.A.G., et al., GenEmbl database, Accession No. AF038548, alignment results (September 1998).
	AS	<u>5</u>	Kondo, H. et al., "Cloning and nucleotide sequence of <i>Bacillus stearothermophilus</i> pyruvate carboxylase," <i>Gene</i> 191:47-50, Elsevier Science Publishers B.V., Amsterdam, Netherlands (May 1997).
	AT	<u>5</u>	Kumar, G.K. et al., "Involvement and Identification of Tryptophanyl Residue at the Pyruvate Binding Site of Transcarboxylase," <i>Biochem.</i> 27:5978-5983, American Chemical Society, Washington D.C. (1988).

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	AL						Yes No
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	6	Lim, F. <i>et al.</i> , "Sequence and Domain Structure of Yeast Pyruvate Carboxylase," <i>J. Biol. Chem.</i> 263:11493-11497, American Society for Biochemistry and Molecular Biology, Inc., Baltimore, MD (1988).
AS	6	Milrad de Forchetti, S.R. and Cazzulo, J.J., "Some Properties of the Pyruvate Carboxylase from <i>Pseudomonas fluorescens</i> ," <i>J. Gen. Microbiol.</i> 93:75-81, Cambridge University Press, Cambridge, England (1976).
AT	6	Momose, H. <i>et al.</i> , "On the Transducing Phages in Glutamic Acid-Producing Bacteria," <i>J. Gen. Appl. Microbiol.</i> 22:119-129, Microbiology Research Foundation, Tokyo, Japan (1976).

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>7</u>	Mukhopadhyay, B. et al., "Purification, Regulation, and Molecular and Biochemical Characterization of Pyruvate Carboxylase from <i>Methanobacterium thermoautotrophicum</i> Strain Δ H," <i>J. Biol. Chem.</i> 273:5155-5166, American Society for Biochemistry and Molecular Biology, Inc., Baltimore, MD (February 1998).
	AS	<u>7</u>	O'Brien, R.W. et al., "Novel Enzymic Machinery for the Metabolism of Oxalacetate, Phosphoenolpyruvate, and Pyruvate in <i>Pseudomonas citronellolis</i> ," <i>J. Biol. Chem.</i> 252:1257-1263, American Society for Biochemistry and Molecular Biology, Inc., Baltimore, MD (1977).
	AT	<u>7</u>	Park, S.M. et al., "Elucidation of anaplerotic pathways in <i>Corynebacterium glutamicum</i> via ^{13}C -NMR spectroscopy and GC-MS," <i>Appl. Microbiol. Biotechnol.</i> 47:430-440, Springer-Verlag, Berlin, Germany (April 1997).

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	8	Peters-Wendisch, P.G. et al., "Phosphoenolpyruvate carboxylase in <i>Corynebacterium glutamicum</i> is dispensable for growth and lysine production," <i>FEMS Microbiol. Lett.</i> 112:269-274, Elsevier/North Holland, Amsterdam, Netherlands (1993).
	AS	8	Peters-Wendisch, P.G. et al., " C_3 -Carboxylation as an anaplerotic reaction in phosphoenolpyruvate carboxylase-deficient <i>Corynebacterium glutamicum</i> ," <i>Arch. Microbiol.</i> 165:387-396, Springer-Verlag, Berlin, Germany (1996).
	AT	8	Peters-Wendisch, P.G. et al., "Pyruvate carboxylase as an anaplerotic enzyme in <i>Corynebacterium glutamicum</i> ," <i>Microbiology</i> 143:1095-1103, Kluwer Academic/Plenum Publishers, Washington, D.C. (April 1997).

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	2	Peters-Wendisch, P.G. <i>et al.</i> , "Pyruvate carboxylase from <i>Corynebacterium glutamicum</i> : characterization, expression and inactivation of the <i>pyc</i> gene," <i>Microbiology</i> 144:915-927, Kluwer Academic/Plenum Publishers, Washington, D.C. (April 1998).
	AS	2	Post, L.E. <i>et al.</i> , "Dissection of the Functional Domains of <i>Escherichia coli</i> Carbamoyl Phosphate Synthetase by Site-directed Mutagenesis," <i>J. Biol. Chem.</i> 265:7742-7747, American Society for Biochemistry and Molecular Biology, Inc., Baltimore, MD (1990).
	AT	2	Reyes, O. <i>et al.</i> , "'Integron'-bearing vectors: a method suitable for stable chromosomal integration in highly restrictive <i>Corynebacteria</i> ," <i>Gene</i> 107:61-68, Elsevier Science Publishers B.V., Amsterdam, Netherlands (1991).

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	AR	<u>10</u>	Scrutton, M.C. and Taylor, B.L., "Isolation and Characterization of Pyruvate Carboxylase from <i>Azotobacter vinelandii</i> OP," <i>Arch. Biochem. Biophys.</i> 164:641-654, Academic Press, New York, NY (1974).
	AS	<u>10</u>	Serwold-Davis, T.M. et al., "Transformation of <i>Corynebacterium diphtheriae</i> , <i>Corynebacterium ulcerans</i> , <i>Corynebacterium glutamicum</i> , and <i>Escherichia coli</i> with the <i>C. diphtheriae</i> plasmid pNG2," <i>Proc. Natl. Acad. Sci. USA</i> 84:4964-4968, National Academy of Sciences of the USA, Washington, D.C. (1987).
	AT	<u>10</u>	Simon, R. et al., "A Broad Host Range Mobilization System For In Vivo Genetic Engineering: Transposon Mutagenesis in Gram Negative Bacteria," <i>Bio/Technol.</i> 1:784-791, Nature Publishing Co., New York (1983).

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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB- CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>11</u>	Sonnen, H. et al., "Characterization of pGAl, a new plasmid from <i>Corynebacterium glutamicum</i> LP-6," <i>Gene</i> 107:69-74, Elsevier Science Publishers B.V., Amsterdam, Netherlands (1991).
	AS	<u>11</u>	Toh, H. et al., "Molecular evolution of phosphoenolpyruvate carboxylase," <i>Plant, Cell and Environ.</i> 17:31-43, Blackwell Scientific Publications, New York, NY (1994).
	AT	<u>11</u>	Tomiooka, N. et al., "Molecular Cloning and Characterization of Ribosomal RNA Genes from a Blue-Green Alga, <i>Anacystis nidulans</i> ," <i>Mol. Gen. Genet.</i> 184:359-363, Springer-Verlag, New York, NY (1981).

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FORM PTO-1449 <u>INFORMATION DISCLOSURE STATEMENT</u>	ATTY. DOCKET NO. 1533.0790002	APPLICATION NO. 10/045,072
	APPLICANT Sinskey et al.	
	FILING DATE January 15, 2002	GROUP 1652

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>12</u>	Tosaka, O. et al., "The Role of Biotin-Dependent Pyruvate Carboxylase in L-Lysine Production," <i>Agric. Biol. Chem.</i> 43(7):1513-1519, Agricultural Chemical Society of Japan, Tokyo, Japan (1979).
	AS	<u>12</u>	Towbin, H. et al., "Electrophoretic transfer of proteins from polyacrylamide gels to nitrocellulose sheets: Procedure and some applications," <i>Proc. Natl. Acad. Sci. USA</i> 76:4350-4354, National Academy of Sciences of the USA, Washington, D.C. (1979).
	AT	<u>12</u>	Vallino, J.J. and Stephanopoulos, G., "Metabolic Flux Distributions in <i>Corynebacterium glutamicum</i> During Growth and Lysine Overproduction," <i>Biotechnol. Bioeng.</i> 41:633-646, Wiley, New York, NY (1993).

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AR	<u>13</u>	Vertès, A.A. et al., "Transposon mutagenesis of coryneform bacteria," <i>Mol. Gen. Genet.</i> 245:397-405, Springer-Verlag, New York, NY (1994).
AS	<u>13</u>	Wexler, I.D. et al., "Primary amino acid sequence and structure of human pyruvate carboxylase," <i>Biochim. et Biophys. Acta</i> 1227:46-52, Elsevier Publishing Co., Amsterdam, Netherlands (1994).
AT	<u>13</u>	Yoshihama, M. et al., "Cloning Vector System for <i>Corynebacterium glutamicum</i> ," <i>J. Bacteriol.</i> 162:591-597, American Society for Microbiology, Baltimore, MD (1985).

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FORM PTO-1449 <u>INFORMATION DISCLOSURE STATEMENT</u>	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%;">ATTY. DOCKET NO. 1533.0790002</td> <td style="width: 50%;">APPLICATION NO. 10/045,072</td> </tr> <tr> <td colspan="2">APPLICANT Sinskey et al.</td> </tr> <tr> <td>FILING DATE January 15, 2002</td> <td>GROUP 1652</td> </tr> </table>	ATTY. DOCKET NO. 1533.0790002	APPLICATION NO. 10/045,072	APPLICANT Sinskey et al.		FILING DATE January 15, 2002	GROUP 1652
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	<u>14</u>	NCBI Entrez, GenBank Report, Accession No. AF038548, Koffas, M.A.G. et al. (December 1997).
	AS	<u>14</u>	NCBI Entrez, GenBank Report, Accession No. Z83018, Cole, S.T. et al. (June 1998).
	AT	<u>14</u>	NCBI Entrez, GenBank Report, Accession No. Z97025, Kunst, F. et al. (June 1998)

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	AR	15	Dialog File 351, Accession No. 12439413, Derwent WPI English language abstract for WO 99/18228.
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